GLP-1 Agonists (Exenatide, Liraglutide, Albiglutide, Dulaglutide)
Criteria for Use

VA Pharmacy Benefits Management Services, Medical Advisory Panel, and VISN Pharmacist Executives

The following recommendations are based on medical evidence, clinician input, and expert opinion. The content of the document is dynamic and will be revised as new information becomes available. The purpose of this document is to assist practitioners in clinical decision-making, to standardize and improve the quality of patient care, and to promote cost-effective drug prescribing. **THE CLINICIAN SHOULD UTILIZE THIS GUIDANCE AND INTERPRET IT IN THE CLINICAL CONTEXT OF THE INDIVIDUAL PATIENT. INDIVIDUAL CASES THAT ARE EXCEPTIONS TO THE EXCLUSION AND INCLUSION CRITERIA SHOULD BE ADJUDICATED AT THE LOCAL FACILITY ACCORDING TO THE POLICY AND PROCEDURES OF ITS P&T COMMITTEE AND PHARMACY SERVICES.**

Exclusion Criteria

- ❑ Type 1 diabetes
- ❑ History of hypersensitivity to GLP-agonist or excipients[1]
- ❑ Patient has end-stage renal disease or CrCl < 30ml/min (for exenatide)[2]
- ❑ Patient with a personal or family history of medullary thyroid carcinoma or with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2)
- ❑ Patient has severe gastrointestinal disease, including gastroparesis or a history of gastric banding or bariatric surgery
- ❑ Patient has a history of pancreatitis[3]

[1] *It is unknown at this time if patients who experienced a hypersensitivity reaction to one GLP-1agonist can safely use another.*

[2] *Exenatide should be used with caution in patients with renal transplantation or when initiating or escalating the dose in patients with moderate renal failure. There is limited experience using liraglutide or dulaglutide in patients with mild, moderate, and severe renal impairment or albiglutide in patients with moderate-severe renal impairment. Use with caution in these patients.*

[3] *Relative exclusions to use include triglyceride level > 500mg/dL, known gallstones with intact gallbladder, and alcohol abuse.*

Inclusion Criteria - Combination with Oral Agents

The following 4 criteria must be met:

- ❑ The provider specializes in diabetes management
- ❑ Patient has type 2 diabetes
- ❑ Patient has not achieved desired HbA1c using combinations of ≥ 2 oral hypoglycemic agents at maximally tolerated doses (this excludes those patients with significant contraindications to SU, metformin, or TZDs that would preclude using at least 2 agents in combination)
- ❑ Patient is not a good candidate for insulin‡

‡ *Insulin allergy, frequent or severe hypoglycemia despite multiple dosage adjustments, special circumstances where the risk of severe hypoglycemia or its potential consequences are significant and/or catastrophic (e.g., workers with frequent rotating shifts and occupations such as truck or bus drivers or heavy machinery operators, etc.)*

Inclusion Criteria - Combination with Insulin (All criteria must be met)

- ❑ The provider specializes in diabetes management
- ❑ Patient has type 2 diabetes
- ❑ Goal A1C has not been achieved
- ❑ Patient is receiving ONE of the following drug therapy regimens†:
    - Basal Insulin + 1-2 oral agents (unless contraindications preclude use of oral agents)
    - Basal Insulin + mealtime insulin therapy ± oral agents
    - GLP-1 agonist + 1-2 oral agents (unless contraindications preclude use of oral agents)

AND 1 of the following:

- ❑ **For those already receiving insulin**†
  Insulin regimen cannot be intensified due to recurrent, unpredictable, or severe hypoglycemia not resolving with adjustment of insulin dose, diet, or exercise OR patient refuses intensification of insulin regimen despite appropriate counseling (valid reason for refusing insulin must be established and documented in the patient medical record)

- ❑ **For those already receiving a GLP-1 agonist**
  Consider discontinuing the GLP-1 agonist upon initiating basal insulin or once the basal insulin dose is stabilized. In the latter case, if glucose control is lost after the GLP-1 agonist is discontinued, initiate mealtime insulin (preferred) or the GLP-1 agonist (if criteria "for those already receiving insulin" is met)

† *Exenatide twice daily, liraglutide, and albiglutide have been studied in combination with long-acting insulin analogs; they have not been studied in combination with prandial insulin. Dulaglutide has been studied in combination with prandial insulin; it has not been studied in combination with basal insulin. Exenatide extended-release has not been studied in combination with any insulin at this time; the manufacturer recommends that it not be used with insulin. None of the GLP-1 agonists have been studied in combination with both basal and prandial insulin.* ***Concomitant use of GLP-1 agonists with regimens containing basal insulin AND prandial insulin (including premixed formulations) is not recommended at this time.***

Dosing

Refer to product package insert for detailed dosing information

Special Considerations

- As part of the Risk Evaluation and Mitigation Strategies (REMS) Program, a medication guide is required to be dispensed with each prescription
- GLP-1 agonists should not be used in combination with meglitinides, alpha-glucosidase inhibitors, or DPP-4 inhibitors
- Monitor patients carefully for the development of pancreatitis after initiation or dose increases of agent. Patients should be instructed to report any unexplained persistent severe abdominal pain which may or may not be accompanied by vomiting to their provider immediately. Discontinue agent if pancreatitis is suspected while using these products. Do not restart if pancreatitis is confirmed.
- Use with caution in patients taking oral medications that require rapid gastric absorption or have a narrow therapeutic index
- There have been post-marketing reports of increased INR with concomitant use of exenatide and warfarin. Monitor INR more frequently after initiation or dosage change of exenatide. Once a stable INR has been achieved, INR can be monitored at the usually recommended interval for warfarin.
- Avoid initiating in individuals whom the potential for dehydration poses a considerable risk (e.g., frail elderly, multiple co-morbid conditions, etc.)
- Case reports suggest that for patients with insulin resistance receiving high-dose insulin (e.g., >1.8 units/kg/day) plus oral medications such as metformin, the addition of a GLP-1 agonist may offer improved glucose control and lowering the insulin dose. A randomized controlled trial is underway.

Follow-up

Discontinue if little to no improvement in glycemic (e.g., A1C, postprandial glucose) goals are seen after 3-6 months of therapy